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Nickel-catalyzed highly chemoselective cocyclotrimerization of arynes with allenes: a novel method for 10-methylene-9,10-dihydrophenanthrenes†

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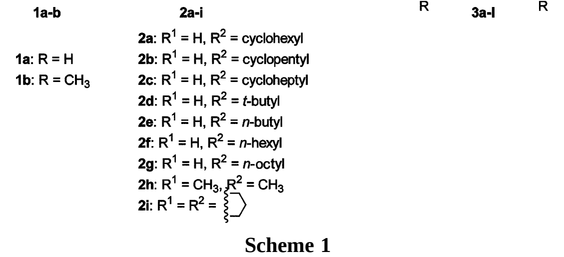
The $NiBr_2$(dppe)–Zn system effectively catalyzes the [2+2+2] cocyclotrimerization of arynes with allenes, leading to 10-methylene-9,10-dihydrophenanthrenes in moderate to good yields. The cocyclotrimerization is highly selective with only the internal double bond of the allenes being involved in the reaction.

The transition-metal mediated [2+2+2] cocyclotrimerization of alkynes is a powerful method for the construction of polycyclic compounds in one step.[1] Although this cycloaddition has been known for decades, the control of both regio- and chemoselectivity remains a great challenge to organic chemists. Recently, the cyclotrimerization of arynes and alkynes has attracted great attention. Perez *et al.* revealed the cyclotrimerization of arynes catalyzed by palladium to give triphenylenes.[2] More recently, both the Perez and the Yamamoto groups reported the cyclotrimerization of benzynes and alkynes catalyzed by palladium complexes leading to the formation of phenanthrene derivatives.[3] Our interest in nickel and cycloaddition chemistry[4,5] encouraged us to explore the possibility of using allenes in the cocyclotrimerization with benzynes. Herein, we wish to report the first example of nickel-catalyzed cocyclotrimerization of two benzynes with an allene, providing an efficient method for the synthesis of 10-methylene-9,10-dihydrophenanthrene derivatives in a highly selective fashion (Scheme 1). Notably, the phenanthrene skeleton is found in a number of biologically active natural products.[6]

Treatment of benzyne precursor (**1a**) with cyclohexylallene (**2a**) in the presence of $NiBr_2$(dppe) (dppe: bis(diphenylphosphino)-ethane), zinc powder and CsF in acetonitrile at 80 °C for 24 h afforded 9-cyclohexyl-10-methylene-9,10-dihydrophenanthrene (**3a**) in 67% yield. The structure of **3a** that is derived from two molecules of **1a** and one molecule of **2a** was confirmed by its ^1H NMR, ^{13}C NMR and mass data. Interestingly, the internal double bond of the allene participates in the cocyclotrimerization reaction and the product having an exocyclic C–C double bond does not undergo isomerization to give the more stable aromatic derivative. The reaction appears highly selective with respect to the double bond of the allene: the other isomer of **3a** with the terminal double bond of the allene being involved in the cocyclotrimerization was not observed.



Scheme 1

To understand the nature of this nickel-catalyzed carbocyclization, the effect of solvent and nickel complex used on the reaction of **1a** with **2a** was investigated. In the absence of either nickel catalyst or zinc powder, no cyclotrimerization product **3a** was observed. $Ni(PPh_3)_2Br_2$ and $Pd(PPh_3)_4$ gave **3a** in 23% and 34% yields, respectively. A substantial amount of triphenylene resulting from homotrimerization of benzyne was observed. $NiBr_2$(dppe) was found to be the best catalyst, producing the desired **3a** in 67% yield and a trace of triphenylene. Solvent was also critical for this catalytic reaction. No reaction occurred in toluene, whereas THF afforded a trace of **3a**. CH_3CN was the best solvent when $NiBr_2$(dppe) was used as the catalyst.

The nickel-catalyzed cocyclotrimerization reaction was successfully extended to various substituted allenes and the results are listed in Table 1. Thus, **1a** reacts with cyclopentyl- (**2b**) and cycloheptylallene (**2c**) to provide the corresponding cocyclotrimerization products **3b–c** in 58 and 64% yields, respectively. Bulky *tert*-butylallene (**2d**) and long chain aliphatic allenes (**2e–g**) underwent [2+2+2] cycloaddition to produce 9,10-dihydrophenanthrene derivatives **3d–g** in good yields (Scheme 1, Table 1, entries 4–7). A small amount of homo-trimerization product ([2+2+2]) of benzyne was observed in all these reactions. No reaction was observed for the cyclotrimerization of benzyne with phenylallene. For the reaction of dimethylallene **2h** with **1a**, two isomers **3h** and **3h′** in 1 : 1.9 molar ratio were observed with a combined yield of 67%. It appears that both C–C double bonds in **2h** are reactive in the reaction. The major isomer **3h′** was produced with the terminal double bond of the allene participating in the cyclotrimerization reaction. Similarly, the reaction of **1a** with disubstituted allene **2i** proceeded to give isomers **3i** and **3i′** in a 2.9 : 1 ratio and total yield of 69%. In contrast to **3h′**, major isomer **3i** in the present case is from the participation of the internal double bond of allene **2i**. The present method can also be applied to the cocyclotrimerization of substituted benzynes. Treatment of 4,5-dimethylbenzyne (**1b**) with cyclohexylallene in the presence of the nickel catalyst furnished dihydrophenanthrene derivative **3j** in 49% yield. In the same fashion, **1b** reacted with *n*-butylallene and *tert*-butylallene to give dihydrophenanthrene derivatives **3k** and **3l** in 46 and 49% yields, respectively.

The foregoing results reveal that all the monosubstituted allenes use their internal C–C double bond for the cocyclotrimerization, but for 1,1-disubstituted allenes both C–C double bonds are involved in the reaction. It is not yet clear why the present catalytic reaction strongly favors the participation of the internal double bond of allenes. However, the observation of products **3h′** and **3i′** from the cycloaddition of the respective terminal double bonds of the 1,1-disubstituted allenes is likely due to the steric effect of the two substituents inhibiting the coordination of the internal double bond of the allene to the nickel center.

Based on the above results and known organometallic chemistry, a plausible mechanism is proposed to account for the formation of 9-methylene-9,10-dihydrophenanthrene products (Scheme 2). The catalytic reaction is likely initiated by the reduction of Ni(II) species to Ni(0) species by zinc metal. Selective coordination of the internal C–C double bond of the allene and then benzyne to the nickel center

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† Electronic supplementary information (ESI) available: synthesis and characterization data of compounds **3**. See http://www.rsc.org/suppdata/cc/b3/b315795d/

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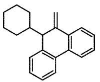
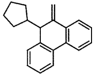
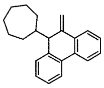
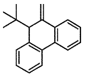
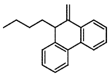
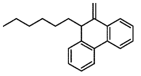
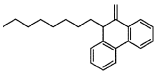
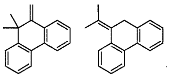
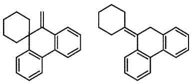
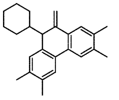
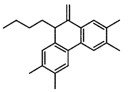
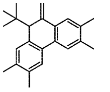
Table 1 Results of nickel-catalyzed cocyclotrimerization of arynes with allenes[a]

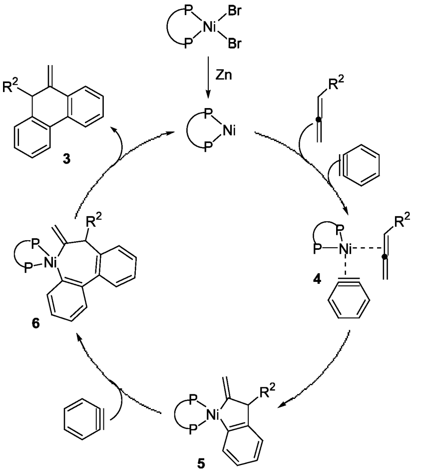
Entry	**1**	**2**	Product	Yield (%)[b]
1	**1a**	**2a**	 **3a**	67
2	**1a**	**2b**	 **3b**	58
3	**1a**	**2c**	 **3c**	64
4	**1a**	**2d**	 **3d**	61
5	**1a**	**2e**	 **3e**	64
6	**1a**	**2f**	 **3f**	60
7	**1a**	**2g**	 **3g**	55
8	**1a**	**2h**	 **3h/3h′**	(1 : 1.9) 67
9	**1a**	**2i**	 **3i/3i′**	(2.9 : 1) 69
10	**1b**	**2a**	 **3j**	49
11	**1b**	**2e**	 **3k**	46
12	**1b**	**2d**	 **3l**	49

[a] Unless stated otherwise, all reactions were carried out using benzyne precursor (**1**) (0.50 mmol), allene (**2**) (1.0 mmol), $NiBr_2$(dppe) (10.0 mol%), CsF (2.0 mmol) and Zn (2.75 equiv.) in CH_3CN (2.0 mL) at 80 °C under N_2 for 24 h. [b] Isolated yields based on benzyne precursor used.

followed by cyclometalation produces nickelacyclopentene intermediate **5**.[7] Coordination of another benzyne and insertion into a Ni(II)–carbon bond gives nickelacycloheptadiene intermediate **6**. Subsequent reductive elimination of **6** affords product **3** and regenerates the Ni(0) catalyst. The other way of cyclometalation of **4** gives intermediate **7**, but this is less likely due to the fact that **7** has a bulky sp^3 carbon attaching the nickel center resulting in strong repulsion between R^2 and the nickel center and dppe ligand (Fig. 1).

An alternative mechanism involves the coordination of two molecules of benzyne to the nickel center to produce a five-membered nickelacyclopentadiene intermediate **8** and insertion of the internal C–C double bond of the allene into a Ni(II)–carbon bond to yield intermediate **6**, followed by reductive elimination to give the final product. This mechanism cannot be totally ruled out.

In conclusion, we have developed a novel methodology for the [2+2+2] cocyclotrimerization of arynes with allenes catalyzed by nickel complexes. This is the first report that allenes can undergo cycloaddition with benzynes in a highly selective fashion to furnish dihydrophenanthrene derivatives in moderate to good yields. Studies to determine the exact mechanistic pathway for this useful reaction are currently underway.



Scheme 2

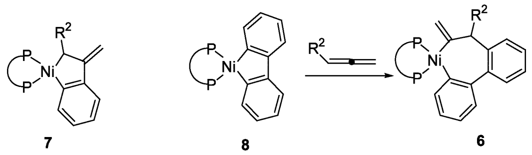


Fig. 1

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